

The Consumption of Well-Done Red Meat and the Risk of Colorectal Cancer

ABSTRACT

Heterocyclic aromatic amines and polycyclic aromatic hydrocarbons are mutagens that are produced in highly cooked meats. A case-control study of 511 patients with colorectal cancer and 500 matched control subjects examined whether consumption of well-done cooked beef is related to the risk of developing large bowel cancer. Approximately 16% of men and women consumed well-done beef, and 50% ate medium-cooked beef. For both sexes, there was no association between consumption of well-done or medium-cooked beef and colorectal cancer. This paper discusses whether questionnaire data accurately reflect dietary intake of heterocyclic aromatic amines and polycyclic aromatic hydrocarbons. (*Am J Public Health.* 1994;84:856-858)

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Introduction

Heterocyclic aromatic amines and polycyclic aromatic hydrocarbons are mutagens that are formed during high-temperature cooking of red meat and, in lesser amounts, white meat and fish.¹ Well-done meat contains 10 times the concentration of heterocyclic aromatic amines than rare meat prepared by the same cooking method.² These amines are mutagenic in bacterial assays³ and have produced colon tumors in laboratory animals.⁴

Only a few epidemiological studies have examined the association between cooked red meats and colon or rectal cancer. In a prospective study of 89 000 US nurses, Willett et al.⁵ reported no association between cooked red meat that was consumed daily and colon cancer; however, they provided no data. In a case-control study, Lyon and Mahoney⁶ found no relationship between consumption of broiled or fried meats and colon cancer. In contrast, a Swedish case-control study of colorectal cancer found an increased risk with total meat intake and a preference for heavily browned meat surface.⁷ Schiffman and Felton⁸ postulated that the degree of doneness of red meat may be an important indicator of heterocyclic aromatic amine intake, and they provided preliminary results from a case-control study of colorectal cancer (n = 50 cases) that showed a significantly increased risk among subjects who consumed well-done red meat. We examined the association between the consumption of well-done beef and colorectal cancer using data from a large case-control study.

Methods

Five hundred eleven patients with histologically confirmed primary cancer of the large bowel (346 with colon cancer, 165 with rectal cancer) were interviewed between 1989 and 1992 in five hospitals. Control patients included 500 subjects matched randomly with each patient by sex, race, hospital, age (within 5 years),

and time of the case interview (within 2 months). Eligible control patients included patients with conditions unrelated to dietary fat and fiber intake, such as joint replacement (9.1%), injuries (8.7%), benign prostatic hyperplasia (7.9%), some musculoskeletal disorders (6.7%), melanoma (4.8%), benign skin diseases (4.0%), ill-defined symptoms (3.6%), renal calculus (3.2%), and hernia (2.8%). The pathology reports of the cases were examined to determine the site and stage of the tumor. More than 90% of both case and control patients who were approached participated in the study.

Data on sociodemographic characteristics, medical history, analgesic use, family history of cancer, smoking, alcohol use, physical activity, vitamin use, and dietary history were collected using a standardized questionnaire administered by trained interviewers. The food frequency section included questions on the major sources of total dietary fat and fiber. For the red meat questions, patients were asked how many times they ate "beef, steaks, roasts or hamburgers" per day, week, or month "during the longest period of your adult life," and whether they ate their beef "well-done, medium or rare."

Relative risks of colorectal cancer associated with well-done beef were calculated using the ratio of discordant case-control pairs for men and women.⁹ Chi-square analysis and 95% confidence intervals (CIs) were calculated to test statistical significance.

Results

Table 1 presents basic sociodemographic characteristics of the study subjects. Case and control patients had similar ages and years of education. A higher proportion of female control pa-

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tients than of female case patients were never married. Male control patients were more likely to have been Jewish and less likely to have been Catholic than male case patients. Approximately 50% of men and women in both groups combined ate medium-cooked beef, and 16% had their beef cooked well-done. The frequency of beef consumption and other potential risk factors were unrelated to the degree of doneness.

Among men, the relative risks for colorectal cancer were 1.15 for consumption of well-done beef (95% CI = 0.6, 2.4) and 1.00 for consumption of medium-cooked beef (Table 2); for rectal cancer only, the relative risk for well-done beef was 2.0 (95% CI = 0.7, 5.9). For women, the relative risks for colorectal cancer were 1.00 for consumption of well-done beef and 0.95 for consumption of medium-cooked beef, with no differences in risk between the colon and the rectum.

Discussion

International correlations between per capita consumption of meat and colorectal cancer rates, as well as epidemiological studies of dietary fat intake, have implicated fat in colon cancer carcinogenesis.¹⁰ Schiffman and Felton⁸ suggest that these correlations may actually reflect intake of heterocyclic aromatic amines. If both fat and amine intake are risk factors for large bowel cancer, then isolating the effects due to amine intake may be difficult in epidemiological studies. The fat content of red meat diminishes with the amount of cooking. Well-done beef contains 36% fat by weight, whereas rare or raw beef contains more than 50% fat according to one study.¹¹ Therefore, the potentially higher risk associated with well-done beef may be counterbalanced by the lower fat content of the meat. On the other hand, low-quality beef with higher fat content is usually cooked more thoroughly than prime cuts and with additional sauces or gravy (which may also contain fat and heterocyclic aromatic amines) to add flavor and texture.

The content of heterocyclic aromatic amines in beef increases substantially with frying time,¹² suggesting that substantial amounts of amines are present only in well-done beef. Schiffman and Felton⁸ report that subjects who consumed well-done beef had a 3.5-fold (95% CI = 1.3, 9.6) increased risk of developing colorectal cancer compared with subjects who ate "rare to medium rare" red meat. The

TABLE 1—Characteristics of 511 Colorectal Case Subjects and 500 Control Subjects

	Men				Women			
	Case (n = 283)		Control (n = 276)		Case (n = 228)		Control (n = 224)	
	No.	%	No.	%	No.	%	No.	%
Age, y								
< 45	13	4.6	15	5.4	11	4.8	12	5.4
45–54	21	7.4	23	8.3	34	14.9	31	13.8
55–64	75	26.5	74	26.8	57	25.0	58	25.9
65–74	124	43.8	136	49.3	87	38.2	98	43.8
> 74	50	17.7	28	10.1	39	17.1	25	11.2
Education, y								
< 12	51	18.0	40	14.5	37	16.2	33	14.7
12	94	33.2	79	28.6	102	44.8	93	41.5
13–15	56	19.8	60	21.7	46	20.2	50	22.3
16	33	11.7	45	16.3	20	8.8	24	10.7
> 16	48	17.0	52	18.8	22	9.7	24	10.7
Marital status								
Single	18	6.4	10	3.6	11	4.8	21	9.4*
Married	228	80.6	216	78.3	127	55.7	110	49.1
Divorced	20	7.1	19	6.9	19	8.3	33	14.7
Widowed	3	1.1	5	1.8	6	2.6	4	1.8
Separated	14	4.9	26	9.4	65	28.5	56	25.0
Religion								
Protestant	61	21.6	49	17.8**	51	22.4	57	25.4
Catholic	130	45.9	110	39.9	91	39.9	80	35.7
Jewish	86	30.4	103	37.3	77	33.8	77	34.4
Other/none	6	2.1	14	5.1	9	3.9	10	4.5
Beef preparation ^a								
Rare	90	32.4	82	30.3	90	40.2	83	37.9
Medium	137	49.3	150	55.3	97	43.3	102	46.6
Well-done	51	18.3	39	14.4	37	16.5	34	15.5

^aExcludes 10 male and 9 female subjects who do not eat red meat; across the columns, bases are 278, 271, 224, and 219.

* $\chi^2_{4df} = 9.14$, $P < .07$; ** $\chi^2_{3df} = 8.7$, $P < .05$.

TABLE 2—Matched-Pair Analysis of Degree of Red Meat Doneness and Colorectal Cancer

Case Subjects	Control Subjects			Relative Risk	95% Confidence Interval
	Rare	Medium	Well-Done		
Men					
Rare	27	42	<u>13</u>	1.00 ^a	...
Medium	<u>42</u>	<u>72</u>	<u>19</u>	1.00	...
Well-done	<u>15</u>	34	5	1.15	0.6, 2.4
Women					
Rare	27	44	<u>12</u>	1.00 ^a	...
Medium	<u>42</u>	<u>33</u>	<u>14</u>	0.95	0.6, 1.5
Well-done	<u>12</u>	15	8	1.00	...

Note. Double-underlined numbers are the discordant pairs for well-done meat. Single-underlined numbers are the discordant pairs for medium-done meat. Table excludes subjects who did not have a matched pair or whose pair did not eat red meat.

^aReference category. An unmatched analysis yielded the same results.

study by deVerdier et al.⁷ shows that consumption of heavily browned meat increases the risk of colorectal cancer.

Lyon and Mahoney⁶ found no significant associations between consumption of broiled or fried meat and risk of colon

cancer. These discrepant study findings may reflect differences in the method of cooking beef (e.g., frying and broiling vs baking) and in the amount of well-done beef consumed. There are little population-based data on beef cooking habits, although one case-control study of 7860 subjects found that men and women ate meat approximately 22 and 18 times per month, respectively,¹³ compared with 13 and 11 times per month, respectively, in this study. The lack of an association in our study may reflect a relatively low intake of highly cooked beef.

Questions on meat consumption frequency tend to have low reliability.^{14,15} It seems intuitive that subjects would respond more accurately to questions on beef doneness, but this needs to be verified. In the Swedish colorectal cancer study (n = 559 cases), a significant risk was found for high "temperature when frying" and "heavily browned" meat surface,⁷ although these definitions may be especially prone to subjective responses. In the study by Schiffman and Felton,⁸ a significant risk was found for well-done red meat compared with both red meat cooked "medium to well" and rare red meat, yet the actual difference in heterocyclic aromatic amine intake between "well-done" and "medium to medium-well" meat may be slight. Further research in this area should consider the opposing risks of a higher amine amount but lower fat content in well-done beef and other meats, and should determine the reliability

and validity of questions on meat cooking habits. □

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